

FORM PTO-1390 (REV 11-2000)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER MUR-8564US	
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371				U.S. APPLICATION NO. (If known, see 37 CFR 1.5) <b>09/763983</b>	
INTERNATIONAL APPLICATION NO. PCT/GB99/03331		INTERNATIONAL FILING DATE 7 October 1999		PRIORITY DATE CLAIMED 7 October 1998	
TITLE OF INVENTION FOAMABLE FORMULATION AND FOAM					
APPLICANT(S) FOR DO/EO/US Thomas Gilchrist and Eilidh Trainer					
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:					
<ol style="list-style-type: none"> <li>1. <input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. 371.</li> <li>2. <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371.</li> <li>3. <input checked="" type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.</li> <li>4. <input checked="" type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (Article 31).</li> <li>5. <input type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2))           <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).</li> <li>b. <input type="checkbox"/> has been communicated by the International Bureau.</li> <li>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</li> </ol> </li> <li>6. <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2))           <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> is attached hereto.</li> <li>b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4).</li> </ol> </li> <li>7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))           <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau).</li> <li>b. <input type="checkbox"/> have been communicated by the International Bureau.</li> <li>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li> <li>d. <input checked="" type="checkbox"/> have not been made and will not be made.</li> </ol> </li> <li>8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</li> <li>9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</li> <li>10. <input type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</li> </ol>					
<b>Items 11 to 20 below concern documents(s) or information included:</b>					
<ol style="list-style-type: none"> <li>11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 U.S.C. 1.97 and 1.98.</li> <li>12. <input checked="" type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</li> <li>13. <input checked="" type="checkbox"/> A <b>FIRST</b> preliminary amendment.</li> <li>14. <input type="checkbox"/> A <b>SECOND</b> or <b>SUBSEQUENT</b> preliminary amendment.</li> <li>15. <input type="checkbox"/> A substitute specification.</li> <li>16. <input type="checkbox"/> A change of power of attorney and/or address letter.</li> <li>17. <input type="checkbox"/> A computer readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 – 1.825.</li> <li>18. <input checked="" type="checkbox"/> A second copy of the published international application under 35 U.S.C. 154(d)(4).</li> <li>19. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).</li> <li>20. <input checked="" type="checkbox"/> Other items or information: Copy of IPE Report</li> </ol>					

U.S. APPLICATION NO. (if known, see 37 CFR 1.5) <div style="font-size: 24pt; font-weight: bold; text-align: center;">09/763983</div>	INTERNATIONAL APPLICATION NO. PCT/GB99/03331	ATTORNEY DOCKET NUMBER MUR-8564US
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21. ☒ The following fees are submitted:

**BASIC NATIONAL FEE (37 CFR 1.492(a)(1) – (5)):**

☐ Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO..... \$1000.00

☒ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO..... \$860.00

☐ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO ..... \$710.00

☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) ..... \$690.00

☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) ..... \$100.00

CALCULATIONS PTO USE ONLY

ENTER APPROPRIATE BASIC FEE AMOUNT =		\$ 860.00	
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).		\$	
CLAIMS	NUMBER FILED	EXTRA NUMBER	RATE
Total claims	24- 20 =	4	X \$18.00
Independent claims	2 - 3 =	0	X \$80.00
MULTIPLE DEPENDENT CLAIM(S) (if applicable) <input type="checkbox"/>		+ \$270.00	\$
TOTAL OF ABOVE CALCULATIONS =		\$ 932.00	
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by ½.		\$	
SUBTOTAL =		\$ 932.00	
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 Months from the earliest claimed priority date (37 CFR 1.492(f)).		\$	
TOTAL NATIONAL FEE =		\$ 932.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property		\$ 40.00	
TOTAL FEES ENCLOSED =		\$ 972.00	
		Amount to be refunded:	\$
		Charged:	\$

a. ☒ Two checks in the amounts of \$932 and \$40, respectively, to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. \_\_\_\_\_ in the amount of \$\_\_\_\_\_ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 18-0350. A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

**NOTE:** Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

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SIGNATURE

Allan Ratner  
NAME

19,717  
REGISTRATION NUMBER

February 28, 2001  
DATE

09/763983

Rec'd PCT/PTO 2.8 FEB 2001

**CERTIFICATE OF MAILING BY "EXPRESS MAIL" (37 CFR 1.10)**Applicant(s): **Thomas Gulchrist and Eilidh Trainer****MUR-8564US**Serial No.  
(to be assigned)Filing Date  
(herewith)

Examiner

Group Art Unit

Invention: **FOAMABLE FORMULATION AND FOAM**

I hereby certify that the following correspondence:

**Transmittal Letter Form PTO-1390 with listed enclosures***(Identify type of correspondence)*

is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 in an envelope addressed to: The Assistant Commissioner for Patents, Washington, D.C. 20231

**February 28, 2001***(Date)***Kristen Foley***(Typed or Printed Name of Person Mailing Correspondence)**(Signature of Person Mailing Correspondence)***EL 736966015 US***("Express Mail" Mailing Label Number)***Note: Each paper must have its own certificate of mailing.**

09/763983

JC02 Rec'd PCT/PTO 28 FEB 2001

MUR-8564US

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Thomas Gilchrist and Eilidh : Interntl Appli. No.:  
Trainer PCT/GB99/03331  
Serial No.: (to be assigned) : Interntl Filing Date:  
Filed: (herewith) : 7 October 1999  
FOR: FOAMABLE :  
FORMULATION AND FOAM

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

S I R :

Preliminary to examination in the United States Patent and  
Trademark Office, please make the following amendments in the above-  
identified application in order to place it in condition for examination.

Amend the specification by inserting before the first line the  
sentence:

This application is the U.S. national phase application of PCT  
International Application No. PCT/GB99/03331 filed 7 October 1999.

**IN THE CLAIMS:**

Please replace claims 3, 5-7, 9-11, 15, 17-19, 21, and 23-24 with the following amended claims:

1                   3.     (Amended) A formulation as claimed in Claim 1 wherein  
2     said gelling agent is alginate, carboxymethylcellulose, collagen, a  
3     polysaccharide, agar, a polyethylene oxide, a glycol methacrylate, gelatin, a  
4     gum, or salts or derivatives of any of these, or mixtures thereof.

1                   5.     (Amended) A formulation as claimed in Claim 1, wherein  
2     said gelling agent has a molecular weight of from 10,000 to 200,000 kDa.

1                   6.     (Amended) A formulation as claimed in Claim 1, wherein  
2     said precipitant is a salt of calcium, zinc, cooper, silver or aluminium; borates;  
3     glyoxal; or amino-formaldehyde pre-condensates.

1                   7.     (Amended) A formulation as claimed in Claim 1 further  
2     containing a foaming agent.

1                   9.     (Amended) A formulation as claimed in Claim 1 wherein  
2     the gelling agent comprises an alginate gel, a carageenan gel or a  
3     carboxymethylcellulose gel and wherein the precipitant is a calcium salt.

1                   10.    (Amended) A formulation as claimed in Claim 1 wherein  
2     the gelling agent comprises carboxymethylcellulose gel and wherein the  
3     precipitant is an aluminium salt.

1           11. (Amended) A formulation as claimed in Claim 1 further  
2 comprising an organic acid in an amount of 0.5 g to 5.0 g per 100 g gelling  
3 agent.

1           15. (Amended) A foam as claimed in Claim 12 wherein said  
2 gelling agent is alginate, carboxymethylcellulose, collagen, a polysaccharide,  
3 agar, a polyethylene oxide, a glycol methacrylate, gelatin, a gum, or salts or  
4 derivatives of any of these, or mixtures thereof.

1           17. (Amended) A foam as claimed in Claim 12, wherein said  
2 gelling agent has a molecular weight of from 10,000 to 200,000 kDa.

1           18. (Amended) A foam as claimed in Claim 12, wherein said  
2 precipitant is a salt of calcium, zinc, copper, silver or aluminium; borates;  
3 glyoxal; or amino-formaldehyde pre-condensates.

1           19. (Amended) A foam as claimed in Claim 12 further  
2 containing a foaming agent.

1           21. (Amended) A process of sterilising a foam for medical or  
2 veterinary use, said process comprising:

3           a) foaming a formulation of Claim 1 and allowing said foamed  
4 formulation to cure;

5           b) treating said foam with precipitant;

6           c) optionally, washing said treated foam;

- 7 d) drying said treated foam; and
- 8 e) sterilising said dried foam by exposure to  $\gamma$ - irradiation or
- 9 ethylene oxide.

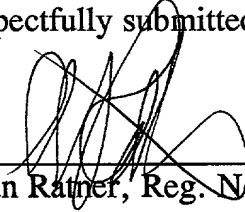
1 23. (Amended) The process of Claim 21 wherein the treated

2 foam is oven dried at temperatures below 100°C.

1 24. (Amended) The process of Claim 21 wherein the foam is

2 immersed in a bath of calcium chloride or calcium citrate solution as precipitant.

Respectfully submitted,

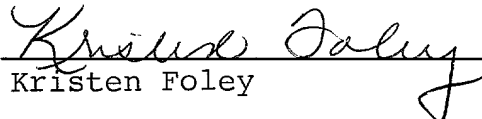
  
Allan Ratner, Reg. No. 19,717  
Attorney for Applicant

AR/lk  
Dated: February 28, 2001  
P.O. Box 980  
Valley Forge, PA 19482  
(610) 407-0700

The Assistant Commissioner for Patents is  
hereby authorized to charge payment to  
Deposit Account No. 18-0350 of any fees  
associated with this communication.

**EXPRESS MAIL** Mailing Label Number: **EL 736966015 US**  
Date of Deposit: **February 28, 2001**

I hereby certify that this paper and fee are being deposited, under 37 C.F.R. § 1.10 and with sufficient postage, using the "Express Mail Post Office to Addressee" service of the United States Postal Service on the date indicated above and that the deposit is addressed to the Assistant Commissioner for Patents, U.S. Patent & Trademark Office, Washington, D.C. 20231, Attn: BOX PCT/EO/US.

  
Kristen Foley

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1                   3.     (Amended) A formulation as claimed in [either one of]  
2     Claim[s] 1 [and 2] wherein said gelling agent is alginate, carboxymethyl-  
3     cellulose, collagen, a polysaccharide, agar, a polyethylene oxide, a glycol  
4     methacrylate, gelatin, a gum, or salts or derivatives of any of these, or mixtures  
5     thereof.

1                   5.     (Amended) A formulation as claimed in [any one of]  
2     Claim[s] 1 [to 4], wherein said gelling agent has a molecular weight of from  
3     10,000 to 200,000 kDa.

1                   6.     (Amended) A formulation as claimed in [any one of]  
2     Claim[s] 1 [to 5], wherein said precipitant is a salt of calcium, zinc, cooper,  
3     silver or aluminium; borates; glyoxal; or amino-formaldehyde pre-condensates.

1                   7.     (Amended) A formulation as claimed in [any one of]  
2     Claim[s] 1 [to 6] further containing a foaming agent.

1                   9.     (Amended) A formulation as claimed in [any one of]  
2     Claim[s] 1 [to 8] wherein the gelling agent comprises an alginate gel, a  
3     carageenan gel or a carboxymethylcellulose gel and wherein the precipitant is a  
4     calcium salt.

1                   10.    (Amended) A formulation as claimed in [any one of]  
2     Claim[s] 1 [to 8] wherein the gelling agent comprises carboxymethylcellulose gel  
3     and wherein the precipitant is an aluminium salt.





- 6                   c)     optionally, washing said treated foam;
- 7                   d)     drying said treated [form] foam; and
- 8                   e)     sterilising said dried foam by exposure to  $\gamma$ - irradiation or
- 9 ethylene oxide.

1                   23.    (Amended) The process of [either one of] Claim[s] 21 [and

2 22] wherein the treated foam is oven dried at temperatures below 100°C.

1                   24.    (Amended) The process of [any one of] Claim[s] 21 [to 23]

2 wherein the foam is immersed in a bath of calcium chloride or calcium citrate

3 solution as precipitant.

1     FOAMABLE FORMULATION AND FOAM

2

3     The present invention is concerned with a foamable  
4     formulation and the foam formed therefrom.

5

6     A wide variety of gels, creams, ointments, lotions and  
7     other formulations are available for application to a  
8     body surface. The exact content of these compositions  
9     will vary depending upon the purpose of application.  
10    For example, a formulation may be applied to clean a  
11    body surface, to promote healing of any wound or  
12    injury, to prevent an exposed wound on the body from  
13    drying out, to prevent infection, etc. In certain  
14    circumstances the composition may include an active  
15    ingredient.

16

17    In our International Patent Application published 13  
18    June 1996 under No WO-A-96/17595 we describe a foamable  
19    formulation which comprises a foamable carrier or  
20    gelling agent, for example an alginate gel, and an  
21    active ingredient, such as a water soluble glass  
22    powder.

23

24    The product described in WO-A-96/17595 represented a  
25    considerable advance over the use of gel or cream.

1 We have now found that by including a precipitant for  
2 the gelling agent, in a slow-release form within the  
3 composition, further improvements with regard to the  
4 setting time of the foam and its stability can be  
5 achieved. In particular, the added stability enables a  
6 pre-foamed pad to be sterilised by irradiation,  
7 ethylene oxide, or other conventional means.

8  
9 Thus, the present invention provides a formulation  
10 comprising a foamed gelling agent combined with a slow-  
11 release precipitant therefor. The gelling agent may be  
12 any agent capable of forming a foam, although  
13 preferably the gelling agent is physiologically  
14 compatible and non-irritant when maintained in contact  
15 with the body surface. The gelling agent may be a gel,  
16 for example a sodium alginate gel, carageenan gel,  
17 sodium carboxymethylcellulose gel or mixtures thereof.

18  
19 The precipitant is desirably intimately admixed  
20 throughout the whole of the foamed gelling agent,  
21 preferably during the foaming process. In certain  
22 circumstances however the presence of the precipitant  
23 on one surface of the foamed gelling agent may be  
24 sufficient to cause stabilisation of the foam.  
25 Examples of precipitants include stabilising  
26 crosslinking agents which render the gelling agent  
27 insoluble. Examples include salts of polyvalent metal  
28 ions such as calcium, zinc, copper, silver or aluminium  
29 as well as borates, glyoxal and amino-formaldehyde  
30 precondensates. In one embodiment, the polyvalent  
31 metal ion may be released from a water-soluble glass  
32 which is admixed into the foamable carrier in  
33 comminuted form. A copper ion-releasing water soluble  
34 glass, a zinc-ion releasing water soluble glass and  
35 mixtures thereof are particularly of interest.

36

1 The role of the precipitant is to stabilise the foamed  
2 gel so that a stable foam is produced. Generally, the  
3 stable foam should be produced within a reasonable time  
4 period since if the precipitant is too slow-acting, the  
5 foam structure will have collapsed prior to  
6 stabilisation. However, a very fast acting precipitant  
7 may not allow sufficient time for the gel to be foamed.  
8 Desirably, the precipitant stabilises the foamed gel  
9 over a time period of 1 minute to 120 minutes,  
10 preferably within 30 minutes, and most preferably  
11 within 15 minutes at ambient temperature. The foam is  
12 considered to be "cured" when it can be lifted and  
13 carefully handled without collapse. The solubility of  
14 the precipitant and hence the setting (cure) time of  
15 the foam may be varied by adjusting the pH of the  
16 composition, especially where the precipitant is based  
17 upon a calcium salt. Generally, the solubility of a  
18 calcium salt will be increased by lowering the pH.  
19 Typical pH adjusters include organic acids such as  
20 acetic, adipic, citric, fumaric, lactic, alginic and  
21 tartaric acids. Usually an amount of 0.5 g to 5 g of  
22 organic acid per 100 gel is sufficient. The organic  
23 acid may be admixed with the precipitant prior to  
24 foaming or, more preferably, may be admixed with the  
25 gelling agent prior to foaming.

26  
27 Suitable precipitants include calcium citrate, calcium  
28 carbonate, calcium phosphate, calcium hydrogen  
29 phosphate ( $\text{CaHPO}_4$ ), aluminium chloride, barium  
30 carbonate, barium phosphate, barium sulphate, barium  
31 chloride and zinc carbonate.

32  
33 Where the gelling agent comprises an alginate gel, a  
34 carageenan gel or a carboxymethylcellulose gel one  
35 preferred precipitant is a calcium salt. Whilst  
36 calcium citrate has been used in the examples, other

1 slowly dissolving calcium salts are also suitable.

2

3 Where the gelling agent comprises  
4 carboxymethylcellulose gel one preferred precipitant is  
5 an aluminium salt.

6

7 In one embodiment the gelling agent and precipitant are  
8 packaged separately and only admixed during the foaming  
9 process or subsequent to foaming.

10

11 Alternatively, the precipitant may be included in a  
12 suspension (e.g. a suspension of calcium citrate and  
13 glycerine) which forms a separate layer on top of the  
14 gelling agent which remains substantially inert during  
15 handling and/or storage. Only once the operator  
16 desires to produce the foam, is the precipitant  
17 intimately admixed with the gelling agent (for example  
18 by shaking the container) and then promptly foamed.  
19 Using the precipitant in suspension form has the  
20 benefit that the suspension is easier to dispense from  
21 a pressurised container than a powder and also provides  
22 for more accurate dosing of unit precipitant per unit  
23 gelling agent.

24

25 Optionally, the formulation may comprise other  
26 additives such as decompactants which promote the  
27 desired foam structure or other foaming agents,  
28 plasticisers, humectants, preservatives, additives,  
29 sequestering agents or active ingredients such as  
30 antimicrobial agents, growth factors, hormones, living  
31 cells, etc.

32

33 The foam may be applied directly to the body area and  
34 allowed to produce a stable foam protective cover, for  
35 example over a wound. With the addition of the  
36 precipitants the cure of the foam is significantly

1 reduced, rendering the product more user friendly.

2  
3 Alternatively, the foam can be produced onto a mould or  
4 other surface area, allowed to cure (for example by air  
5 drying or oven drying) and then applied to the body  
6 surface as a dressing. A foam sheet of this type is a  
7 preferred embodiment of the invention since it exhibits  
8 sufficient stability for easy handling whilst retaining  
9 a moist surface to promote wound healing. Optionally,  
10 the foam may be applied about a substrate (for example  
11 cloth, mesh, non-woven pad of alginate fibres, nylon,  
12 rayon, polylactid acid, polyglycolic acid,  
13 polycaprolactone or biocompatible glass fibres) which  
14 are then integrated into the foam pad produced.

15  
16 As an example, the foam may be used to treat  
17 dermatological conditions (including psoriasis, atopic  
18 and allergic eczema). It may be convenient in this  
19 embodiment for the foam to deliver an active ingredient  
20 normally used to alleviate such conditions, for example  
21 a steroid such as hydrocortisone.

22  
23 In another embodiment the foam may be used to treat  
24 burns or scalds, including sunburn.

25  
26 In another embodiment the foam may be applied  
27 cosmetically, and for example may include skin  
28 moisturising agents, nutritional agents and growth  
29 factors suitable to promote skin regeneration. A foam  
30 intended for cosmetic use may include colorants or  
31 pigments so that the foam may be applied to the skin as  
32 a cosmetic or to disguise any blemishes in the skin.

33  
34 The foam may be used prophylactically. In particular a  
35 foam containing a UV blocking agent may be applied to  
36 exposed areas of the skin to protect it from the

1 effects of the sun.

2

3 The formulation of the invention is applied to the body  
4 site of interest in the form of a foam and it is  
5 therefore essential that the composition undergoes a  
6 foaming process before application to the body. In the  
7 foaming process gas is forced into or is formed within  
8 the formulation to entrap small bubbles of gas therein,  
9 thereby forming the foam. Any suitably gas or gas  
10 producing system can be used to produce the foam.

11 Mention may be made of butane and nitrous oxide, but  
12 other gases like air, nitrogen, hydrofluorocarbons such  
13 as HFC134a or 227, hydrocarbons like propane,  
14 isopropane or a mixture thereof, are also suitable.  
15 Conveniently the foam may be produced by conventional  
16 means such as by using aerosol technology.

17

18 The formulation according to the present invention may  
19 be stored in any convenient container until required.  
20 Generally, the container will be designed to preserve  
21 the sterile nature of the formulation. Conveniently  
22 the container will be provided with means to foam the  
23 composition when required. Details are given in WO-A-  
24 96/17595. A two can packaging and dispensing system,  
25 as described in our co-pending UK Patent Application No  
26 9823029.5 (a copy of which is filed herewith), may be  
27 used to dispense the foam according to the present  
28 invention.

29

30 Generally, the foam will be produced from sterile  
31 ingredients.

32

33 Prior to the foaming process, the foamable carrier is  
34 preferably in the form of a gel. The gel may be  
35 sterilised and this is generally desirable where the  
36 foam is intended for medical use. Usually,



1 sterilisation will take place by autoclaving the  
2 formulation, since this is currently the most economic  
3 means of achieving sterilisation. Autoclaving at  
4 temperatures of from 100°C to 125°C for under ½ hour is  
5 normally sufficient. Generally, the autoclaving  
6 process should be as mild as possible, whilst being  
7 sufficient to sterilise the formulation. For example,  
8 autoclaving at temperatures of about 121°C for 15-20  
9 minutes is acceptable. The autoclaved formulation may  
10 then be foamed when cool. It is also possible,  
11 however, to sterilise the formulation by other means,  
12 for example by  $\gamma$ -irradiation or e-beam irradiation. It  
13 has been found that autoclaving the gel may cause the  
14 MW of the foamable carrier to be slightly reduced.  
15 Consequently it may be desirable to select a foamable  
16 carrier having a higher MW than that ultimately  
17 required.

18  
19 The foam forms an air-tight cover around any wound or  
20 injury to which it is applied, and this prevents that  
21 area from drying out and may also combat infection.  
22 The advantages of applying a topical product in the  
23 form of a foam include:

- 24
- 25 1. Easy rapid application,
- 26 2. Conforms to surface irregularities,
- 27 3. Insulates the wound,
- 28 4. Cools the tissues,
- 29 5. Offers antibacterial action to prevent
- 30 infection,
- 31 6. Biocompatibility with tissue,
- 32 7. Suitable for use as a vehicle for the
- 33 administration of pharmaceutical agents,
- 34 and/or
- 35 8. Maintains a moist environment.
- 36

1 Generally, the formulation of the present invention  
2 will be applied directly to the body site of interest  
3 in the form of a foam, the foam being produced from any  
4 suitable device (such as an aerosol) immediately before  
5 application. It is, however, possible for a quantity  
6 of the foamed formulation to be produced and then  
7 applied onto the body site by any suitable means, for  
8 example by hand or by spatula. This method may be  
9 required for wounds having a narrow opening.

10

11 As stated above, the foam may also be produced on a  
12 suitable surface and then allowed to dry to produce a  
13 stable foam sheet which can be handled as described  
14 above without deterioration. Generally, the production  
15 of the sheet will take place under sterile conditions  
16 or may be sterilised after production. In the prior  
17 described foam product of WO-A-96/17595, it was not  
18 possible to provide a foamed pad product and then  
19 sterilise the pad by conventional means such as  $\gamma$ -  
20 irradiation, since it was found that the foam structure  
21 deteriorated during sterilisation. With the inclusion  
22 of the precipitant however, sterilisation of the  
23 pad is possible both by  $\gamma$ -irradiation, ethylene oxide  
24 sterilisation or other conventional means. This  
25 represents a very considerable advantage over the prior  
26 art product.

27

28 The foam sheet is generally produced by foaming the  
29 foamable carrier in the presence of the precipitant and  
30 allowing the foam to cure, usually by simply exposing  
31 the foam to the atmosphere to air dry at ambient  
32 temperature. Optionally the foam may be dried at  
33 elevated temperatures, for example may be oven dried.  
34 Desirably, the cure time of the foam is 40 minutes or  
35 less at ambient temperature and preferably the foam  
36 cures within 15 minutes, for example within 10 minutes.

1 Where the foam sheet is to be sterilised, it is  
2 advantageous to pre-treat the sheet prior to  
3 sterilisation in order to further stabilise the sheet.  
4 The difficulty with sterilising any foam of the type  
5 described is that the foam structure tends to  
6 deteriorate and collapse during the sterilisation  
7 process. The pre-treatment of the sheet preferably  
8 involves impregnating the sheet with further  
9 precipitant. Conveniently, this may entail immersing  
10 the sheet in a bath of the precipitant or of a solution  
11 of the precipitant. For example, the sheet may be  
12 immersed in a bath of calcium chloride or calcium  
13 citrate. To ensure that the precipitant penetrates  
14 into the centre of the foam sheet, the sheet may be  
15 gently squeezed whilst immersed in the bath.  
16 Generally, immersion of the sheet for a short period of  
17 time, such as 2 to 3 minutes, is sufficient. The sheet  
18 may then be removed from the bath of precipitant,  
19 washed in a mixture of de-ionised water and glycerine  
20 to enhance moisture content and then dried. The  
21 stabilised foam sheet may then be sterilised by gamma  
22 radiation or through use of ethylene oxide.

23  
24 The ratio of de-ionised water : glycerine in the wash  
25 stage is preferably 19:1 by volume.

26  
27 The treated foam sheet is desirably oven dried at  
28 relatively low temperatures, for example 100°C or less,  
29 preferably approximately 35°C.

30  
31 In a preferred embodiment the foamable carrier includes  
32 a combination of copper and zinc ions, optionally in  
33 the form of water soluble glass(es). We have found  
34 that a foam containing appropriate quantities of these  
35 metal ions are particularly resistant to the  
36 deleterious effects of sterilisation. We hypothesise

1 that the copper and zinc ions act as scavenger of free  
2 radicals produced in the foam during sterilisation and  
3 which are, we believe, responsible for the breakdown in  
4 structure of the foam. Additionally, both copper and  
5 zinc ions have a radioprotective effect. Consequently,  
6 we consider that any material known for its use as a  
7 free radical scavenger and/or as a radioprotectant may  
8 likewise exhibit a protective effect on the foam  
9 structure during sterilisation.

10

11 Optionally the manufacture of a prefoamed product may  
12 envisage a continuous foaming process. The sheet may  
13 be divided into a convenient size and may be packaged.  
14 Optionally the foam sheet may be produced on contoured  
15 surface so that it is moulded to a pre-determined  
16 shape.

17

18 Examples of suitable foamable gelling agents for use in  
19 the composition of the present invention include (but  
20 are not limited to) alginate and derivatives thereof,  
21 carboxymethylcellulose and derivatives thereof,  
22 collagen, polysaccharides (including, for example,  
23 dextran, dextran derivatives, pectin, starch, modified  
24 starches such as starches having additional carboxyl  
25 and/or carboxamide groups and/or having hydrophillic  
26 side-chains, cellulose and derivatives thereof), agar  
27 and derivatives thereof (such as agar stabilised with  
28 polyacrylamide), carageenan, polyethylene oxides,  
29 glycol methacrylates, gelatin, gums such as xanthum,  
30 guar, karaya, gellan, arabic, tragacanth and locust  
31 bean gum. Also suitable are the salts of the  
32 aforementioned carriers, for example, sodium alginate.  
33 Mixtures of any of the aforementioned gelling agents  
34 may also be used, as required.

35

36 Preferred foamable gelling agents include alginate,

1 carageenan, carboxymethylcellulose, the derivatives and  
2 salts thereof and mixtures of any of these. Alginate  
3 (the derivatives or salts thereof, such as sodium and  
4 calcium alginate) are especially preferred. Foamable  
5 gelling agents having a molecular weight of from 10,000  
6 to 200,000 kDa are preferred, especially over 100,000  
7 kDa, for example 150,000 to 200,000 kDa, may be used.

8  
9 The formulation may further comprise a foaming agent,  
10 which promotes the formation of the foam. Any agent  
11 having a surfactant character may be used. The  
12 surfactants may be cationic, non-ionic or anionic.  
13 Examples of suitable foaming agents include cetrimide,  
14 lecithin, soaps, silicones and the like. Commercially  
15 available surfactants such as Tween™ are also suitable.  
16 Cetrimide (which additionally has an anti-bacterial  
17 activity) is especially preferred.

18  
19 The formulation of the present invention (and thus the  
20 foam) may be used to deliver pharmaceutically active  
21 agents, in particular to deliver such agents in a  
22 controlled release manner. Mention may be made of:

23  
24 Antiseptics, Antibacterials and Antifungal agents,  
25 such as Chlorhexidine, acetic acid, polynoxylin,  
26 povidone iodine, mercurochrome phenoxyethanol,  
27 acridene, silver nitrate, dyes eg brilliant green,  
28 undecanoic acid, silver sulphadiazine, silver  
29 proteins and other silver compounds,  
30 metronidazole, benzaclonium chloride;

31  
32 Nutritional agents, such as vitamins and proteins;

33  
34 Growth factors and healing agents, including  
35 Ketanserin a serotonomic blocking agent;

36

1        Living Cells;

2

3        Enzymes include streptokinase and streptodormase;

4

5        Elements - zinc, selenium, cerium, copper,  
6        manganese, cobalt, boron, arsenic, chromium  
7        silver, gold, gallium;

8

9        Charcoal;

10

11       Desloughing and Debridng agents such as  
12       hypochlorite and hydrogen peroxide;

13

14       Astringents including potassium permanganate;

15

16       Antibiotics exemplified by neomycin and framycetin  
17       sulphate, sulfamylon, fusidic acid, mupirocin,  
18       bacitracin, gramicidin.

19

20       In addition the formulation of the present invention  
21       may further comprise other conventional additives such  
22       as plasticisers and humectants (such as glycerol,  
23       propane-1,2-diol, polypropylene glycol and other  
24       polyhydric alcohols), free radical scavengers to  
25       stabilise against the effects of sterilisation by  
26       irradiation, viscosity-adjusting agents, dyes and  
27       colorants, and the like.

28

29       Several experiments including comparatives tests have  
30       been made in order to demonstrate some of the  
31       advantages of the new compositions of the invention.  
32       Of course the embodiments described hereinbelow are  
33       submitted in order to better describe the invention and  
34       not to limit its scope.

35

36

**EXAMPLE 1****PROCEDURE FOR MANUFACTURE OF UNIT BATCH (100 g) of  
ALGINATE GEL**

Typically the alginate gels are made according to the following process:

1. De-ionised (DI) water is measured and poured into mixing vessel 1.
2. Desired amounts of suitable alginate (for example Keltone or Manucol) and glycerine are weighed using a calibrated balance, reading to 2 decimal places.
3. Alginate and glycerine are mixed together in a beaker until no lumps remain.
4. The whole alginate/glycerine mix is added very slowly to the water.
5. Once all the alginate/glycerine has been added to the water, the mixture is stirred until a smooth gel has formed.

Several different alginate gels have been made according the above process. They differ and are referred to by the amount of alginate (for example Keltone) used. For example the alginate gel code 6½ has the following composition:

GEL CODE	6½
DI Water	80 ml
Glycerine	25.22 g
Keltone	6.5 g
Unit Batch Wt	111.72 g

The above composition can be varied to include other

weights of alginate, which would be reflected in the gel code number. For example a composition having 8g alginate (plus 80ml DI water and 25.22g glycerine) would be designated gel code 8. Analogous gel codes are used when other gel formers (eg carageenan or CMC) are substituted for the alginate in the above composition.

In one embodiment, the gelling agent may be present in the form of a suspension, for example a suspension in glycerine. To avoid diluting the gelling agent, the gelling agent suspension may be made up with less glycerine such that the total quantity of glycerine present in the gelling agent mixture and in the precipitant suspension adds up to the required amount. For example, the glycerine in the gelling agent mixture and precipitant suspension may be varied as follows:

Glycerine per 80 ml DI water and 6 g alginate (g)	Glycerine in precipitant suspension (g)
25.22	0
23.0	2.22
20.0	5.22
18.22	7.0
15.0	10.22

The above is illustrated with respect to a gel code 6 composition, but the division of glycerine may be made for other gel code compositions, and is also not limited to the specific volumes illustrated above.



1     **PROCEDURE FOR FOAM PRODUCTION**

2

3     The propellant used to produce the foam can be  
4     compressed gases such as air, nitrogen, nitrous oxide  
5     or air, hydrofluorocarbons such HFC134a or 227 or  
6     hydrocarbons including propane, isopropane, n-butane,  
7     isobutane and 2-methylbutane.

8

9     Propellant vapour pressure can range from 0 to 110 PSIG  
10    at 70°C although the preferred range is 20 to 70 PSIG.  
11    Values within this range can be achieved for example by  
12    blending the three hydrocarbons propane, isobutane and  
13    butane. Calor Aerosol Propellants (CAP) sold by Calor  
14    Gas Ltd Slough may be used as propellant gas, when a  
15    blend of propane, isobutane and butane is used the  
16    proportions can be as follows:

17

18	<u>Grade</u>	<u>Propane %</u>	<u>Isobutane %</u>	<u>n Butane%</u>
19	CAP 30	11	29	60
20	CAP 40	22	24	54
21	CAP 70	55	15	30

22

23    A foam according to the invention can advantageously be  
24    produced following the following process:

- 25    1.   100 g of a gel according to the invention is  
26        poured to an aerosol canister.
- 27    2.   2.5 g of calcium citrate (food grade) is  
28        added to the canister.
- 29    3.   A valve is crimped onto the canister.
- 30    4.   Air is purged from the canister.
- 31    5.   4.5 g of propellant gas is added into the  
32        canister (65:35 CAP 40 : Isopentane  
33        propellant) and an actuator is positioned on  
34        the valve.
- 35    6.   The canister is shaken vigorously for 20-30  
36        seconds.

1       7.    The canister is inverted and the foam dispensed.

2

3       EXAMPLE 2

4       Using a range of water-based gel formulations detailed  
5       below tests were done to improve the "setting" time and  
6       stability of the gel and its foam.

7

8       Preferred alginate compositions have an amount of  
9       alginate ranging from 5-9g in the composition set out  
10      in Example 1. Preferred alginates are Keltone HV and  
11      Manucol DMF.

12

13      Experiment 1. Gel Code 6½ Alginate gel and foam mixed  
14      with calcium citrate compared to Gel Code 6½ alginate  
15      gel alone

16

17      Foamed gel with calcium citrate

18      2.5 g calcium citrate was added to 100 g of gel and the  
19      foamed gel was spread out onto plastic sheeting. The  
20      resultant foam pad was liftable in 15 minutes.

21

22      Foamed gel without calcium citrate

23      The above experiment was reproduced by foaming the gel  
24      on its own as described above. The "setting" time of  
25      the foam was 10 hours.

26

27      The experiments were repeated using 100 g unfoamed gel  
28      with and without calcium citrate. Similar setting  
29      times to those observed for the foamed gels were  
30      obtained (15 minutes and 10 hours respectively) before  
31      the gel pads were liftable.

32

33      Conclusion: Calcium citrate speeds up and controls the  
34      setting time of the gel and the foam.

35

36      Experiment 2. Gel Code 8 Alginate gel mixed with water

1 soluble glass (WSG) containing phosphate and boron  
2 compared to gel code 8 alginate gel alone.

3

4 The WSG was comprised as follows:

5 28.5M% CaO

6 3M% Ag

7 5M% B<sub>2</sub>O<sub>3</sub>

8 18.5M% MgO

9 45M% P<sub>2</sub>O<sub>5</sub>

10

11 Foamed gel with WSG

12 2.5 g of WSG was mixed with 100 g gel and the foamed  
13 mixture was spread out onto plastic sheeting. The  
14 resultant foam pad was liftable in 120 mins.

15

16 Foamed gel without WSG

17 The above experiment was repeated by foaming the gel on  
18 its own. The "setting" time of the foam was  
19 approximately 10 hours.

20

21 The experiments were repeated using 100 g unfoamed gel  
22 with and without WSG. Similar setting times to those  
23 observed for the foamed gels were obtained (120 minutes  
24 and 10 hours respectively) before the gel pads were  
25 liftable.

26

27 Conclusion: WSG speeds up and controls the setting  
28 time of the gel and the foam.

29

30 **Experiment 3. Gel Code 4 Carageenan gel mixed with**  
31 **calcium citrate compared to gel code 4 gel alone**

32

33 Foamed gel with calcium citrate

34 3 g of calcium citrate was mixed with 100 g gel and the  
35 foamed mix was spread out onto plastic sheeting. The  
36 resultant foam pad was liftable in 120 mins.

1     Foamed gel without calcium citrate

2     The above experiment was repeated by foaming gel on its  
3     own as described above. The "setting" time of the foam  
4     was 10 hours.

5  
6     The experiments were repeated using 100 g unfoamed gel  
7     with and without calcium citrate. Similar setting  
8     times to those observed for the foamed gels were  
9     obtained (120 minutes and 10 hours respectively) before  
10    the gel pads were liftable.

11  
12    **Experiment 4. Gel Code 4½ Carageenan gel and gel code**  
13    **6½ alginate gel mixed with calcium citrate compared to**  
14    **gel code 4½ carageenan gel and gel code 6½ alginate gel**  
15    **alone**

16  
17    Foamed gel with calcium citrate

18    2.5 g of calcium citrate was mixed with (50 g alginate  
19    and 50 g carageenan) gel and the foamed mix was spread  
20    out onto plastic sheeting. The resultant foam pad was  
21    liftable in 15 mins.

22  
23    Foamed gel without calcium citrate

24    The above experiment was repeated by foaming the mixed  
25    gel on its own. The "setting" time of the foam pad was  
26    10 hours.

27  
28    The experiments were repeated using 100 g unfoamed gel  
29    with and without calcium citrate. Similar setting  
30    times to these observed for the foamed gels were  
31    obtained (120 minutes and 10 hours respectively) before  
32    the gel pads were liftable.

33  
34    **Experiment 5. Gel Code 6½ Alginate gel mixed with**  
35    **calcium citrate and added bentone IPM gel**

36

1 2.5 g calcium citrate was added to 100 g of gel with 1g  
2 bentone IPM gel, admixed in an aerosol canister and  
3 dispensed therefrom as a foam onto a plastic surface.  
4 The resultant foam pad was liftable in 12 minutes.  
5 Bentone IPM gel is an admixture of isopropyl myristate,  
6 sterealkonium hectorite and propylene carbonate.

7  
8 Conclusion: Calcium citrate and bentone gel control  
9 the setting time of the foam. Bentone gel also acts as  
10 a reological agent and assists in the smoothness of  
11 delivery from the can.

12  
13 **Experiment 6. Gel Code 6½ Alginate gel mixed with**  
14 **calcium citrate and added cetrimide**

15  
16 2.5 g calcium citrate was added to 100 g of alginate  
17 gel with 1g cetrimide in an aerosol canister and foamed  
18 onto a plastic surface. The resultant foam pad was  
19 liftable in 15 minutes.

20  
21 Conclusion: Calcium citrate speeds up the setting time  
22 of the foam. Cetrimide increases the cell structure of  
23 the product.

24  
25 **Experiment 7. Gel Code 6½ Alginate gel mixed with**  
26 **calcium citrate and added Tween 20**

27  
28 2.5 g Calcium citrate was added to 100 g of alginate  
29 gel with 1g Tween 20 and foamed onto a plastic surface.  
30 The resultant foam pad was liftable in 12 minutes.

31  
32 Conclusion: Calcium citrate speeds up the setting time  
33 of the gel. The additive Tween 20 gave a much smoother  
34 delivery and an airier foam. Tween 80, 60 and 40 were  
35 also tried and all assisted in the delivery and product  
36 cell structure.

1     **Experiment 8. Gel Code 4 Carboxymethyl cellulose and gel**  
2     **code 6½ alginate gel mixed with calcium citrate**  
3     **compared to the gel alone**

4  
5     2.5 g calcium citrate was added to (50 g CMC & 50 g  
6     alginate gel) and then the mixture was foamed onto a  
7     plastic surface. The resultant foam pad was liftable  
8     in 25 minutes. The gel foamed on its own was liftable  
9     overnight (approx. 10 hours).

10

11     **Experiment 9. Gel Code 4 Carboxymethyl cellulose gel**  
12     **mixed with aluminium chloride compared with the gel**  
13     **alone**

14

15     2 g aluminium chloride was mixed with 100 g CMC gel.  
16     The gel was spread onto a plastic surface. The  
17     resultant gel was liftable instantly. The gel alone was  
18     liftable overnight (approx. 10 hours).

19

20     **Experiment 10. Gel Code 6 Alginate gel mixed with**  
21     **citric acid compared to gel code 6 alginate gel alone**

22

23     2.5 g of citric acid was mixed with 100 g alginate gel  
24     and the mix was spread out onto plastic sheeting. The  
25     resultant gel pad was liftable in 120 mins. 100 g of  
26     the gel alone was spread onto plastic sheeting and the  
27     resultant pad was only liftable overnight (approx. 10  
28     hours).

29

30

31

32

33

34

35

36

Experiment 11. Gel Code 6% Alginate gel was mixed with the following powders on a 100 g gel: 2.5 g powder basis

Powder	Results as a gel	Results as a foam
Calcium Chloride	Gel pad was formed instantly	Fast setting foam
Calcium Sulphate	Gel pad formed reasonably quickly	Foam set reasonably quickly
Aluminium Chloride	Gel pad formed instantly	Fast setting foam
Calcium Metaborate	Gel pad formed instantly	Fast setting foam

Experiment 12. Setting performances of a foam of a gel code 6% alginate gel as a function of the amounts of calcium citrate.

Batch No	Amount of calcium citrate per 100 g gel	Result
DM02 210798	4 g	Not dispensed - set in can
DM03 210798	3 g	Very difficult to dispense. 9½ minutes to set.
DM04 210798	2.5 g	Easier to dispense than above. 18½ minutes to set
DM05 210798	2.25 g	Taking longer to set. 20 minutes.
DM02 200798	2 g	Setting time - 40 minutes

1     **Experiment 13. Gel Code 6½ alginate gel with calcium**  
2     **citrate and isopentane.**

3  
4     100g gel code 6½ alginate gel was admixed with varying  
5     amounts of calcium citrate (2 to 4g), added to  
6     isopentane and mixed thoroughly before being spread  
7     onto a glass sheet. The isopentane vaporises at  
8     ambient temperatures and boils off through the gel  
9     leaving a foam pad of similar consistency to those  
10    produced by dispersion from an aerosol can. After  
11    half-an-hour the foam pads were liftable.

12  
13    **EXAMPLE 3**

14  
15    **A. Gel code 5 alginate gel mixed with calcium citrate**  
16

17    The gel was prepared by mixing together alginate (5g  
18    Keltone HV), 20g glycerine and 80ml de-ionised water.  
19    5.22g glycerine was then added to 2.5g calcium citrate  
20    and a suspension of precipitant was created. The  
21    resultant gel and the suspension of precipitant were  
22    added to an aerosol can and a valve fitted. The can  
23    was purged of air, filled with 4.5g CAP 40 butane,  
24    shaken and dispensed. The foam produced was well mixed  
25    and set in 15 minutes.

26  
27    **B. Gel code 5 alginate gel mixed with calcium citrate**  
28

29    Experiment A was repeated using the same weight of  
30    Manucol LKX (5g) instead of Keltone HV. The resultant  
31    foam set within 12 minutes.

32  
33    **C. Gel code 5 alginate gel mixed with calcium citrate**  
34

35    The gel was prepared by mixing together alginate (5g  
36    Keltone HV), 20g glycerine and 80ml de-ionised water.



1 5.22g glycerine was then added to 2.5g calcium citrate  
2 and a suspension of precipitant was created. The  
3 resultant gel was added to the bottom can of the two  
4 can packaging system (see our co-pending UK Patent  
5 Application No 9823029.5) and the suspension or  
6 precipitant was added to the top can. The cans were  
7 prepared in the usual way. The two can packaging  
8 system was activated and the foam was dispensed. The  
9 foam produced was well mixed and set in 15 minutes.

10

11 **D. Gel code 5 alginate gel mixed with calcium citrate**

12

13 Experiment C was repeated using the same weight of  
14 Manucol LKX instead of Keltone HV. The resultant foam  
15 set within 12 minutes.

16

17 The set foam from A, B, C and D were then further  
18 processed by first immersing the foam in a solution of  
19 2.5% calcium chloride solution for 2 minutes, rinsing  
20 in de-ionised water and then finally rinsing in a 1%  
21 glycerine solution. The foam pads were then dried in  
22 the oven at 35°C and packaged in sterilisable pouches.

23

24 The resultant sterilised pads were compared with can  
25 reference 2 below (see Example 4). The foams produced  
26 in the two can system had a more even pore size  
27 throughout compared to those made in a one can system.  
28 Comparing the suspension with the powder/gel mix showed  
29 no difference in the structure of the final product.

30

31 **EXAMPLE 4**

32

33 A 1 litre batch of gel code 5 alginate gel was  
34 manufactured. Nine bottom cans of a two can packaging  
35 system as described in our co-pending UK Patent  
36 Application No 9823029.5 were filled with 100g gel in

1 each. Nine top cans were made up with varying powders  
2 as detailed below. The cans were prepared in their  
3 usual way. The two can packaging system was activated  
4 and the foam was dispensed.  
5  
6 Once cured the foams were processed by varying a) the  
7 concentration of the calcium chloride immersion  
8 solution and b) the final wash concentration of the  
9 glycerine solution. All samples were halved and then  
10 oven dried at 40°C. The first half sample was removed  
11 after 8 hours and the second half after 16 hours. Once  
12 the foam pads had been processed they were packaged in  
13 EtO sterilisable airtight packaging as soon as they  
14 came out of the oven. The samples were sent for EtO  
15 sterilisation and examined on their return.

Can Ref	Top Can Component	Ca Chloride Conc.	Glycerine Sol Conc.	Drying Time	Description of Alginate Pad After EtO Sterilisation
1	2.5 g Ca Citrate	1%	1%	8 hrs	Flexible, soft & sponge-like
				16 hrs	Flexible, soft & sponge-like
2	2.5 g Ca Citrate	2.5%	1%	8 hrs	Moist, flexible & sponge-like
				16 hrs	Flexible, soft & sponge-like
3	2.5 g Ca Citrate	5%	1%	8 hrs	Dry pad with limited flexibility
				16 hrs	Dry pad with limited flexibility
4	2.5 g Ca Citrate	2.5%	2%	8 hrs	Moist, flexible, soft & sponge-like
				16 hrs	Moist, flexible, soft & sponge-like
5	2.5 g Ca Citrate	2.5%	2.5%	8 hrs	Moist, flexible, sponge-like pad
				16 hrs	Moist, flexible, sponge-like pad
6	2.5 g Ca Citrate	2.5%	5%	8 hrs	Moist, flexible, soft & sponge-like
				16 hrs	Moist, flexible, soft & sponge-like
7	2 g Ca Citrate 2 g Activated Charcoal	2.5%	5%	8 hrs	Moist, flexible, soft & sponge-like
				16 hrs	Moist, flexible, soft & sponge-like
8	2 g Ca Citrate 2 g Cu/Zn WSG	2.5%	5%	8 hrs	Moist, flexible, soft & sponge-like
				16 hrs	Moist, flexible, soft & sponge-like
9	2.5 g Ca Citrate 2 g Povidone Iodine	2.5%	5%	8 hrs	Moist, flexible, soft & sponge-like
				16 hrs	Moist, flexible, soft & sponge-like

**EXAMPLE 5****Experiment A**

A 600 g batch of gel code 5 was made up using Manucol DMF as the gelling agent. This batch was split into six equal parts and inserted into the bottom can of a dual can aerosol system. The top cans were made up containing 1.5 g calcium citrate and varying amounts of alginic acid ( $\frac{1}{2}$  g increments from 0 to  $2\frac{1}{2}$  g). Once preparation was complete the cans were foamed out simultaneously and the setting time for each foam was recorded.

Can Number	Gel Weight	Calcium Citrate Weight	Alginic Acid Weight	Setting Time
1	100 g	1.5 g	0 g	20 mins
2	100 g	1.5 g	0.5 g	16 mins
3	100 g	1.5 g	1.0 g	14 mins
4	100 g	1.5 g	1.5 g	10 mins
5	100 g	1.5 g	2.0 g	9 mins
6	100 g	1.5 g	2.5 g	8 mins

**Experiment B**

Three 100 g batches of gel code 5 was made up using Manucol DMF as the gelling agent with alginic acid incorporated (0 g, 1 g and 2 g added). Each batch was filled into bottom cans and top cans were made up containing 1.5 g calcium citrate. Once preparation complete the cans were foamed out simultaneously and the setting times for each can recorded.

Can Number	Gel Weight	Calcium Citrate Weight	Alginic Acid Weight	Setting Time
7	100 g	1.5 g	1 g	8 mins
8	100 g	1.5 g	2 g	6 mins
9	100 g	1.5 g	0 g	20 mins

CLAIMS

1. A physiologically acceptable formulation for application to a body as a foam, said formulation comprising a foamable gelling agent and a slow-release precipitant therefor, wherein said slow-release precipitant is combined with said gelling agent during the foaming thereof and stabilises the foamed form of the gelling agent.
2. A formulation as claimed in Claim 1 wherein said precipitant is packaged separately to said gelling agent prior to foaming.
3. A formulation as claimed in either one of Claims 1 and 2 wherein said gelling agent is alginate, carboxymethylcellulose, collagen, a polysaccharide, agar, a polyethylene oxide, a glycol methacrylate, gelatin, a gum, or salts or derivatives of any of these, or mixtures thereof.
4. A formulation as claimed in Claim 3 wherein said gelling agent is alginate, carboxymethyl-cellulose, carageenan gel, the derivatives or salts thereof, or mixtures thereof.
5. A formulation as claimed in any one of Claims 1 to 4, wherein said gelling agent has a molecular weight of from 10,000 to 200,000 kDa.
6. A formulation as claimed in any one of Claims 1 to 5, wherein said precipitant is a salt of calcium, zinc, copper, silver or aluminium; borates; glyoxal; or amino-formaldehyde pre-condensates

- 1 7. A formulation as claimed in any one of Claims 1 to  
2 6 further containing a foaming agent.  
3
- 4 8. A formulation as claimed in Claim 7 wherein said  
5 foaming agent is cetrimide, lecithin, a soap,  
6 silicone, a surfactant or the like.  
7
- 8 9. A formulation as claimed in any one of Claims 1 to  
9 8 wherein the gelling agent comprises an alginate  
10 gel, a carageenan gel or a carboxymethylcellulose  
11 gel and wherein the precipitant is a calcium salt.  
12
- 13 10. A formulation as claimed in any one of Claims 1 to  
14 8 wherein the gelling agent comprises  
15 carboxymethylcellulose gel and wherein the  
16 precipitant is an aluminium salt.  
17
- 18 11. A formulation as claimed in any one of Claims 1 to  
19 10 further comprising an organic acid in an amount  
20 of 0.5 g to 5.0 g per 100 g gelling agent.  
21
- 22 12. A physiologically acceptable foam comprising a  
23 foamed gelling agent stabilised by a precipitant.  
24
- 25 13. The foam as claimed in Claim 12 in the form of a  
26 cured foam sheet.  
27
- 28 14. A foam as claimed in Claim 12 wherein said  
29 precipitant is packaged separately to said gelling  
30 agent prior to foaming.  
31
- 32 15. A foam as claimed in any one of Claims 12 to 14  
33 wherein said gelling agent is alginate,  
34 carboxymethylcellulose, collagen, a  
35 polysaccharide, agar, a polyethylene oxide, a  
36 glycol methacrylate, gelatin, a gum, or salts or

- 1 derivatives of any of these, or mixtures thereof.  
2
- 3 16. A foam as claimed in Claim 15 wherein said gelling  
4 agent is alginate, carboxymethyl- cellulose,  
5 carageenan gel, the derivatives or salts thereof,  
6 or mixtures thereof.  
7
- 8 17. A foam as claimed in any one of Claims 12 to 16,  
9 wherein said gelling agent has a molecular weight  
10 of from 10,000 to 200,000 kDa.  
11
- 12 18. A foam as claimed in any one of Claims 12 to 17,  
13 wherein said precipitant is a salt of calcium,  
14 zinc, copper, silver or aluminium; borates;  
15 glyoxal; or amino-formaldehyde pre-condensates  
16
- 17 19. A foam as claimed in any one of Claims 12 to 18  
18 further containing a foaming agent.  
19
- 20 20. A foam as claimed in Claim 19 wherein said foaming  
21 agent is cetrimide, lecithin, a soap, silicone, a  
22 surfactant or the like.  
23
- 24 21. A process of sterilising a foam for medical or  
25 veterinary use, said process comprising:  
26
- 27 a) foaming a formulation of Claims 1 to 11 and  
28 allowing said foamed formulation to cure;  
29
- 30 b) treating said foam with precipitant;  
31
- 32 c) optionally, washing said treated foam;  
33
- 34 d) drying said treated form; and  
35  
36



1 e) sterilising said dried foam by exposure to  $\gamma$ -  
2 irradiation or ethylene oxide.

3

4 22. The process of Claim 21 wherein said treated foam  
5 is washed in a de-ionised water/glycerine mixture  
6 prior to drying.

7

8 23. The process of either one of Claims 21 and 22  
9 wherein the treated foam is oven dried at  
10 temperatures below 100°C.

11

12 24. The process of any one of Claims 21 to 23 wherein  
13 the foam is immersed in a bath of calcium chloride  
14 or calcium citrate solution as precipitant.

15

# Declaration and Power of Attorney For Patent Application

## English Language Declaration

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled FOAMABLE FORMULATION AND FOAM, the specification of which is attached hereto unless the following box is checked:



was filed on 7 October 1999 as PCT International Application Number PCT/GB99/03331.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR § 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. §119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)

Priority Not Claimed

9821736.7

GB

7 October 1998

(Number)

(Country)

(Day/Month/Year Filed)

☐

9907065.8

GB

27 March 1999

(Number)

(Country)

(Day/Month/Year Filed)

☐

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below.

\_\_\_\_\_  
(Application Number)

\_\_\_\_\_  
(Filing Date)

\_\_\_\_\_  
(Application Number)

\_\_\_\_\_  
(Filing Date)

I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s), or 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Number) (Filing Date) (Status - patented, pending, abandoned)

(Application Number) (Filing Date) (Status - patented, pending, abandoned)

**POWER OF ATTORNEY:** As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith:

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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Inventor's signature X Thomas Gilchrist Date X 7 February 2001

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☐ Additional inventors are being named on separately numbered sheets attached hereto.